Palladium-Catalyzed Formylation of Organic Halides with Carbon Monoxide and Tin Hydride

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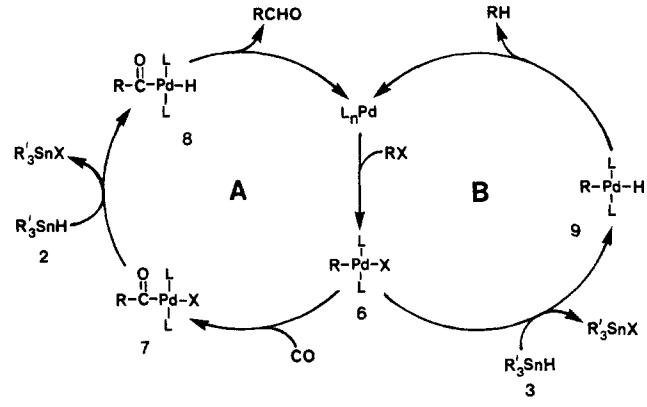
Abstract: The palladium-catalyzed formylation of a wide variety of organic substrates (aryl iodides, benzyl halides, vinyl iodides, vinyl triflates, and allylic halides) with tin hydride and carbon monoxide gives good yields of aldehydes under mild conditions (50 °C, 1-3 atm of CO, and 2.5-3.5-h reaction times) and tolerates a number of functional groups. A competitive side reaction, the direct reduction of the halide or triflate, could be minimized by the slow addition of tributyltin hydride and higher pressures of carbon monoxide. In general, electron-donating or -withdrawing substituents on the aryl halide have no effect on the formylation reaction; however, a *p*-nitro substituent causes significant reduction in the yield of aldehyde. Yields are diminished by steric hindrance about the electrophile. The formylation of unsymmetrical allyl halides is regioselective, taking place at the less substituted allylic position, with retention of geometry at the allylic double bond. Retention of the double bond geometry also is observed in the formylation of vinyl iodides.

Although a variety of methods are available for the preparation of aldehydes from carboxylic acids and their derivatives, most involve metallic hydrides as reducing agents.[1] Hydrogen[2] (Rosenmund reduction) or silicon hydrides,[3] in the presence of a palladium catalyst, have been successfully employed in reducing acid chlorides to aldehydes. The conversion of a number of organic halides into aldehydes has been accomplished by using carbon monoxide and hydrogen (1:1, 1200-1500 psi) at 80-100 °C.[4] Aryl halides can be formylated under lower carbon monoxide pressures when silicon hydrides are utilized as the hydride source.[5] These routes to aldehydes are not without their disadvantages, however, since the scope of the reaction is somewhat limited. Other reducible functionality in the molecule cannot usually be tolerated, and overreduction of the aldehyde to the alcohol is often observed, the product alcohol often reacting further.

Tributyltin hydride is a relatively mild metal hydride reducing reagent, which has been employed for the preparation of aldehydes. Although the uncatalyzed reduction of acid chlorides by tributyltin hydride yields a mixture of aldehydes and esters[6] (from overreduction of the aldehyde to alcohol), the introduction of a palladium catalyst directs the reduction nearly exclusively to the aldehyde.[7] The reaction occurs under mild conditions and in the presence of other reducible groups. However, this transformation is limited by the availability of the corresponding acid chloride and the intolerance of the reactive substrate to other functionality. The suggested mechanism[7] for this catalytic reaction involves sequential oxidative addition of the acid chloride to the palladium(0) catalyst, to yield an acylhalopalladium(II) complex, followed by transmetalation with tin hydride, and finally reductive elimination to afford the aldehyde and regenerate the palladium(0) catalyst.

Scheme I



The proposed catalytic cycle is analogous to that which describes the palladium-catalyzed conversion of acid chlorides to ketones by tetraorganotin reagents.[8] Recently, a palladium-catalyzed coupling of organic electrophiles (halides and triflates) with organotin reagents in the presence of carbon monoxide has been developed to yield ketones.[9] Presumably, this carbonylative coupling reaction requires the formation of an acylpalladium(II) intermediate, which is the same intermediate complex in the catalytic cycle proposed for the reduction of acid chlorides with organotin hydrides.[7]

These results suggested that palladium would catalyze the conversion of various organic electrophiles to aldehydes in the presence of carbon monoxide and a tin hydride reagent. In a preliminary communication,[10] we showed that such a procedure does allow the formylation of a number of organic halides, providing a versatile new method of aldehyde synthesis which overcomes the drawbacks of acid chloride starting materials.

Results and Discussion

Reaction Conditions. The reaction between iodobenzene (**1**) and tributyltin hydride (**2**), added via syringe pump, at 50 °C in tetrahydrofuran (THF) in the presence of 3.7 mol % of tetrakis(triphenylphosphine)palladium(0), $Pd(PPH_3)_4$ (**3**), under 15

(1) Boron and aluminum derivatives see: (a) Babler, J. H.; Invergo, B. J. *Tetrahedron Lett.* **1981**, *21*, 11-14. (b) Brown, H. C.; Krishnamurthy, S. *Tetrahedron* **1979**, *35*, 567-607. (c) Malek, J.; Cerny, M. *Synthesis* **1972**, 217-234. (d) Reinheckel, H.; Haage, K.; Jahnke, D. *Organomet. Chem. Rev., Sect. A* **1969**, *4*, 47-136.

(2) (a) Mosettig, E.; Mozingo, R. *Org. React. (N.Y.)* **1948**, *4*, 362-377. (b) Peters, J. A.; Van Bekkum, H. *Recl. Trav. Chim. Pays-Bas* **1971**, *90*, 1323-1325.

(3) (a) Citron, J. D. *J. Org. Chem.* **1969**, *34*, 1977-1979. (b) Dent, S. P.; Eaborn, C.; Pidcock, A. *J. Chem. Soc., Chem. Commun.* **1970**, 1703-1704. (c) Dent, S. P.; Eaborn, C.; Pidcock, A. *J. Chem. Soc., Dalton Trans.* **1975**, 2646-2648.

(4) Schoenberg, A.; Heck, R. F. *J. Org. Chem.* **1974**, *39*, 3327-3331.

(5) (a) Pri-Bar, I.; Buchman, O. *J. Org. Chem.* **1984**, *49*, 4009-4011. (b) Kikukawa, K.; Totoki, T.; Wada, F.; Matsuda, T. *J. Organomet. Chem.* **1984**, *270*, 283-287.

(6) (a) Kupchik, E. J.; Kiesel, R. J. *J. Org. Chem.* **1966**, *31*, 456-461. (b) Kuivila, H. G. *Synthesis* **1970**, 499-509. (c) Lusztyk, J.; Lusztyk, E.; Maillard, B.; Ingold, K. U. *J. Am. Chem. Soc.* **1984**, *106*, 2923-2931.

(7) (a) Guibe, F.; Four, P.; Riviere, H. *J. Chem. Soc., Chem. Commun.* **1980**, 432-433. (b) Four, P.; Guibe, F. *J. Org. Chem.* **1981**, *46*, 4439-4445.

(8) (a) Milstein, D.; Stille, J. K. *J. Org. Chem.* **1979**, *44*, 1613-1618. (b) Labadie, J. W.; Stille, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 6129-6137.

(9) (a) Goure, W. F.; Wright, M. E.; Davis, P. D.; Labadie, S. S.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 6417-6422. (b) Merrifield, J. H.; Godschalx, J. P.; Stille, J. K. *Organometallics* **1984**, *3*, 1108-1112. (c) Crisp, G. T.; Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 7500-7506.

(10) Baillargeon, V. P.; Stille, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 7175-7176.

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Table I. Condition Study: Conversion of Iodobenzene to Benzaldehyde[a]

entry	temp, °C	solv	R_3SnH, R	addition time, h	catalyst	products, % GC yield		
						PhCHO (**4**)	PhH (**5**)	PhI (**1**)
1	50	THF	Bu	2.5	$Pd(PPh_3)_4$ (**3**)	85	15	0
2	25	THF	Bu	2.5	**3**	62	37	1
3	0	THF	Bu	2.5	**3**	9	19	72
4[b]	50	THF	Bu	2.5	**3**	93	7	0
5[c]	50	THF	Bu	2.5	**3**	93	7	0
6	50	Tol	Bu	2.5	**3**	93	7	0
7	50	PhH	Bu	2.5	**3**	60	*d*	4
8	50	$CHCl_3$	Bu	2.5	**3**	*e*	*e*	97
9	30	Et_2O	Bu	2.5	**3**	7	44	49
10	50	THF	Bu	0.5	**3**	38	62	0
11	50	THF	Bu	1.0	**3**	71	29	0
12	50	THF	Bu	6.5	**3**	84	16	0
13	50	THF	Bu	2.5[f]	**3**	69	14	17
14	50	Tol	Bu	2.5	$Pd(dba)_2$[g]	97	3	0
15[h]	50	acetone	Bu	2.5	$Pd(dba)_2$	0	*e*	99
16	50	THF	Bu	2.5	*i*	0	12	88
17	50	Tol	Me	2.5	*i*	0	10	90
18	0	Tol	Me	2.5	**3**	35	6	59
19	25	Tol	Me	2.5	**3**	35	65	0
20	50	Tol	Me	2.5	**3**	86	14	0

[a] General conditions: 1 atm of CO, 1 mmol of PhI in 3–5 mL of solvent, 3.5–4.0 mol % of palladium catalyst, 0.6–0.8 mmol of ethylbenzene or toluene (as internal GC standard), and 1.1 mmol of R_3SnH diluted to 10 mL with the appropriate solvent. [b] 2 atm of CO. [c] 3 atm of CO. [d] Product unobservable due to GC peak overlap with solvent. [e] Trace. [f] Bu_3SnH diluted to 1 mL with THF. [g] Two equivalents of triphenylphosphine per palladium was added. [h] The same results were obtained by using $Pd(CH_3CN)_2Cl_2$ in either acetone or HMPA. [i] No added palladium.

psi of carbon monoxide afforded an 85% yield of benzaldehyde (**4**) and a 15% yield of benzene (**5**). The products observed in

$$\underset{\mathbf{1}}{PhI} + CO + \underset{\mathbf{2}}{Bu_3SnH} \xrightarrow[\underset{\mathbf{3}}{Pd(PPh_3)_4}]{THF,\ 50\ ^\circ C} \underset{\mathbf{4}\ 85\%}{PhCHO} + \underset{\mathbf{5}\ 15\%}{PhH}$$

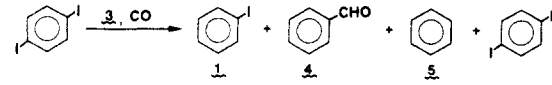
this reductive carbonylation reaction can be explained by two overlapping catalytic cycles[7,9] (Scheme I). Each catalytic cycle begins with the oxidative addition of **1** (RX = PhI) to the palladium(0) catalyst to give the common alkyliodopalladium(II) complex (**6**). In the presence of carbon monoxide, intermediate **6** is able to undergo migratory CO insertion to give the acyliodopalladium(II) complex (**7**) of cycle A. A transmetalation reaction between **7** and tributyltin hydride (**2**) gives an acylhydridopalladium(II) complex (**8**), which is then able to undergo reductive elimination to yield **4** and regenerate the reactive palladium(0) complex.

The undesired side product of halide reduction is produced as illustrated in cycle B. In competition with the CO insertion, tributyltin hydride (**2**) can undergo transmetalation with complex **6**, thus giving an alkylhydridopalladium(II) complex (**9**). Complex **9** can then undergo reductive elimination to give the reduced product and regenerate the palladium(0) catalyst.

The effects of varying the reaction conditions were studied, particularly with respect to the competing reduction reaction (Table I). Reduced temperatures slowed the reaction, leaving greater amounts of unreacted starting material and favoring the reduction of iodobenzene (**1**) to benzene (**5**) (entries 1–3, Table I). Higher carbon monoxide pressures resulted in a more competitive CO insertion process (cycle A, Scheme I) over the direct transmetalation (cycle B, Scheme I), and yields of benzaldehyde were increased (entries 1, 4, 5, Table I). Although conducting the formylation reaction in toluene provided a slightly higher yield of benzaldehyde than when the reaction was run in THF, benzene, chloroform, and ether were poor solvents for this reaction. Addition times shorter than 2.5 h afforded higher yields of benzene with correspondingly lower yields of aldehyde, while longer addition times gave the same results as a 2.5-h addition (entries 1, 10–12, Table I). Reducing the dilution volume of tributyltin hydride (**2**) from 10 to 1 mL, but still using a 2.5-h addition time, resulted in incomplete consumption of iodobenzene and a lower yield of aldehyde (entries 1, 13, Table I).

Employing bis(dibenzylideneacetone)palladium(0), $Pd(dba)_2$, with 2 equiv of triphenylphosphine per palladium, instead of catalyst **3**, gave a higher yield of benzaldehyde under 1 atm of CO (entries 1, 14, Table I). Conducting the formylation reaction with "ligandless" catalysts[11] failed to give any aldehyde (entry 15, Table I). Treatment of iodobenzene with tributyltin hydride in the absence of any palladium catalyst under carbon monoxide did not afford any aldehyde; however, a 12% yield of benzene was obtained (entry 16, Table I). Thus, some reduced product may be formed via a non-palladium-catalyzed route. A similar result was obtained upon treatment of iodobenzene with trimethyltin hydride (**10**). At 50 °C, the formylation of iodobenzene using trimethyltin hydride (**10**) gave product yields equivalent to those obtained with tributyltin hydride (**2**); however, at lower temperatures, much more benzene was obtained from the reduction of iodobenzene (entries 1–3, 19–20, Table I). Due to difficulty in the preparation and storage of trimethyltin hydride, tributyltin hydride was the reagent of choice.

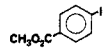
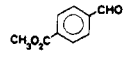
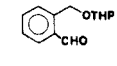
Formylation of Aryl Halides. The formylation reaction is quite general and can be applied to a variety of aryl halides (Table II). Because bromobenzene could not be formylated readily under the reaction conditions (entry 2, Table II), bromoiodobenzenes and chloroiodobenzenes were preferentially formylated at the iodide position to give the corresponding halobenzaldehyde (entries 3–5, Table II). Treatment of 1,4-diiodobenzene under the typical reaction conditions did not afford the desired dialdehyde, terephthalaldehyde; rather, the diiodide was only partially consumed to give iodobenzene (**1**), benzaldehyde (**4**), and benzene (**5**). Two equivalents of tributyltin hydride consumed the 1,4-diiodobenzene, but only benzaldehyde and benzene were obtained.



Substituted aryl iodides generally were formylated in high yields, regardless of the electronic nature of the substituent. Although aryl iodides with electron-donating substituents formylated well under 1 atm of CO, those with electron-withdrawing substituents required 3 atm of CO in order to minimize the competitive reduction side reaction. Even at the higher pressures, the *p*-nitro substituent was an exception, causing considerable reduction and affording *p*-nitrobenzaldehyde in low yield (entries 13, 14, Table II). Substituents at the ortho position adversely affected the

(11) Beletskaya, I. P. *J. Organomet. Chem.* **1983**, *250*, 551–564.

Table II. Formylation of Aryl Halides

ENTRY	RX	Rxn Cond[b]	Products - % GC Yield (% Isol Yield) RCHO	RH	RX
1		A	 93	7	0
2		B[c]	 2	28	70
3		D	 87 (70)	d	0
4		D	 94 (78)	6	0
5		D	 91 (77)	9	0
6		A	 11	56	34
7		D	 91 (90)	9 (8)	0
8		D	 88 (68)	12	0
9		D	 (21)	(73)	0
10		D	 95 (41)	5	0
11		A	 0	0	95
12		A	 7	69	15
13		A	 9	84	0
14		B	38 (20)	62	0
15		C	 76 (62)	22	0
16		A	99	e	0
17		A	 70 (28)	e	0
18		A	 100 (77)	0	0
19		A	 (76)	12	0
20		A	 (55)[f]	20	0
21		D	 (72)	e	0
22		D	 (60)	e	0

[a] General conditions: 1–3 mmol of substrate in 3–10 mL of solvent, 50 °C, 3.5–4.0 mol% of $Pd(PPh_3)_4$, 0.5–1.5 mmol of ethylbenzene or toluene (as internal GC standard where appropriate), and 2.5–3.5-h addition of 1.1 equiv of Bu_3SnH diluted to 10 mL with the appropriate solvent. [b] Specific reaction conditions: A = Tol, 1 atm of CO; B = Tol, 3 atm of CO; C = THF, 1 atm of CO; D = THF, 3 atm of CO. [c] Heated to 106 °C. [d] 4% yield of bromobenzene, 10% yield of benzene. [e] Yield not determined. [f] Product isolated as a 1:3 mixture of the free aldehyde and ring-closed hemiacetal.

Table III. Formylation of Benzyl Halides

ENTRY	RX	Rxn Cond[b]	Products - % GC Yield (% Isol Yield) RCHO	RH
1		C	66	21
2		C	75	12
3		D	94 (17)[c]	6
4		D	(67)	c

[a] General conditions: 1–3 mmol of substrate in 3–10 mL of solvent, 50 °C, 3.5–4.0 mol % of $Pd(PPh_3)_4$, 0.5–1.5 mmol of ethylbenzene or toluene (as internal GC standard where appropriate), and 2.5–3.5-h addition of 1.1 equiv of Bu_3SnH diluted to 10 mL with the appropriate solvent. [b] Specific reaction conditions: A = Tol, 1 atm of CO; B = Tol, 3 atm of CO; C = THF, 1 atm of CO; D = THF, 3 atm of CO. [c] Product isolated and characterized as the 2,4-DNP derivative.

formylation reaction, presumably due to steric hindrance, and led to decreased yields of aldehyde (entries 9, 17, Table II).

The formylations of 2- and 3-iodobenzyl alcohols demonstrated the tolerance of this carbonylative procedure to an alcohol function (entries 19, 20, Table II). In the conversion of 2-iodobenzyl alcohol (**11**), the formylation reaction apparently occurred more rapidly than ring closure to the corresponding lactone, **12**.[12]

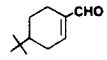
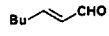
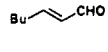
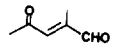
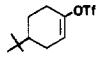
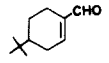
An aryl iodide containing an *o*-ethyleneamine function was examined as a possible starting material for preparing imines via this formylation reaction. However, treatment of *N*-acetyl-2-iodo-4,5-dimethoxy-β-phenethylamine[13] did not afford the corresponding aldehyde or lactam. Aryl triflates do not undergo the formylation reaction under the standard reaction conditions for the carbonylation of vinyl triflates (vide supra).

Formylation of Benzyl Halides. Benzyl halides gave good yields of substituted acetaldehydes under 1 atm of carbon monoxide; however, raising the pressure to 3 atm significantly improved the yields of formylated product (Table III). The gentle nature of the carbonylation procedure was demonstrated by the conversion of 3-furfuryl bromide to the corresponding aldehyde in good yield with no further reaction of the furan ring or the acetaldehyde group (entry 4, Table III).

This new formylation reaction was not synthetically useful for either a neopentyl iodide or an alkynyl iodide. The neopentyl group is apparently too sterically hindered, resulting in exclusive reduction of neopentyl iodide in low conversion. The alkynyl iodide afforded a mixture of products, as the triple bond is susceptible

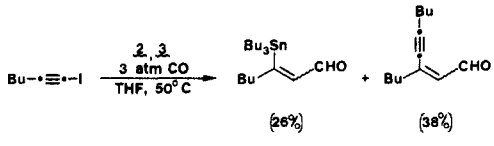
(12) Cowell, A.; Stille, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 4193–4198.
(13) Kihara, M.; Kobayashi, S. *Chem. Pharm. Bull.* **1978**, *26*, 155–160.

Table IV. Formylation of Vinyl Iodides and Vinyl Triflates

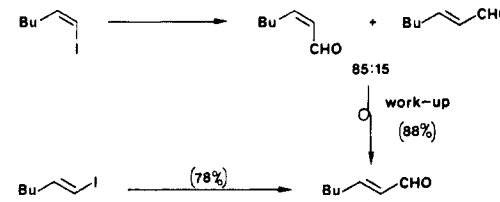
ENTRY	RX	Rxn Cond[b]	Products - % GC Yield RCHO	RH	[% Isol Yield] RX
1		A	 89 [53]	c	0
2		D	 98 [59]	2	0
3		C[d]	 85 [35]	c	0
4		D	 [78]	c	0
5		D	 [88][e]	c	0
6		A	 20	69	0
7		B	84 [43]	18	0
8		B	 0	100	0
9		B	 95 [51]	c	0
10		C[f]	 55	45	0
11		D[f]	98 [67]	2	0
12		D[f]	 96 [50]	4	0
13		C[f]	 89 [53]	8	3
14		D[f]	13	2	85 [54]
15		C[f]	 27 [26][g]	4	69
16		D[f]	1	0	96 [48]

[a] General conditions: 1–3 mmol of substrate in 3–10 mL of solvent, 50 °C, 3.5–4.0 mol % of $Pd(PPh_3)_4$, 0.5–1.5 mmol of ethylbenzene or toluene (as internal GC standard where appropriate), and 2.5–3.5-h addition of 1.1 equiv of Bu_3SnH diluted to 10 mL with the appropriate solvent. [b] Specific reaction conditions: A = Tol, 1 atm of CO; B = Tol, 3 atm of CO; C = THF, 1 atm of CO; D = THF, 3 atm of CO. [c] Yield not determined. [d] Me_3SnH used. [e] Crude product indicated an 85:15 ratio of cis to trans product. [f] 2–3 equiv of lithium chloride added. [g] Product isolated and characterized as the 2,4-DNP derivative.

to a variety of side reactions under the reaction conditions, such as addition of tributyltin hydride to the triple bond to give a vinyltin compound.[14]



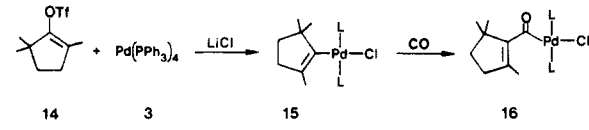
Formylation of Vinyl Iodides and Vinyl Triflates. Vinyl iodides were formylated to α,β-unsaturated aldehydes in good yields (entries 1–5, Table IV).



The geometric integrity of the olefin was preserved during the formylation reaction. However, isomerization of the olefin occurred during workup, and only the thermodynamic product was isolated (entries 4, 5, Table IV). Mixed results were obtained with β-iodo enones (entries 6–9, Table IV). Although 3-iodo-2-cyclohexenone and (*E*)-4-iodo-3-penten-2-one were formylated in high yields (entries 7, 9, Table IV), 3-iodocyclopentenone (entry 8, Table IV) was reduced exclusively, and (*Z*)-4-iodo-3-penten-2-one afforded a complex mixture of products.

For the preparation of α,β-unsaturated aldehydes, vinyl triflates were preferred to vinyl iodides. Although the reaction required the addition of lithium chloride, vinyl triflates were formylated as well as the vinyl iodides, yet triflates offered the advantages of greater stability and regiospecific control during their preparation.[15] 4-*tert*-Butyl-1-cyclohexenyl triflate was formylated in better yield under 3 atm of carbon monoxide than 1 atm (entries 10, 11, Table IV). However, as the steric hindrance was increased about the vinyl triflate, a decrease in yield was observed (entries 11, 14, 16, Table IV). Although 1 atm of carbon monoxide was less desirable for 4-*tert*-butyl-1-cyclohexenyl triflate, lowering the CO pressure to 1 atm for the hindered cases increased the yields of formylated products significantly (entries 13–16, Table IV). However, even at 1 atm, the very sterically hindered 2,5,5-trimethyl-1-cyclopentenyl triflate (**14**) was incompletely consumed, affording a low yield of formylated product. Vinyl triflate **14** has been successfully carbonylated to a ketone in 33 h by a similar palladium-catalyzed carbonylation reaction and a tetaorganotin reagent.[9c] By contrast, formylation reactions were typically conducted over only 2.5–3.5 h. However, even the slow addition of tributyltin hydride (**2**) to **14** over 21 h did not give different results than the 3.5-h addition.

The reaction of vinyl triflate **14**, with a stoichiometric amount of tetrakis(triphenylphosphine)palladium(0) (**3**), was carried out in order to examine the oxidative addition and migratory CO insertion steps in the formylation reaction. A solution consisting



of **14**, 1 equiv of **3**, and an excess of lithium chloride was heated in THF under argon for 1 h. Analysis of the mixture by ^{31}P NMR showed a signal at 23.3 ppm, corresponding to an alkylpalladium(II) complex.[8b] Passing CO through the solution for 5 min produced a ^{31}P NMR signal at 15.1 ppm, characteristic of an acylpalladium(II) complex,[8b] with the loss of the 23.3 ppm signal. Under both 1 and 3 atm of CO, the IR spectrum of the acyl complex exhibited the acylpalladium band[16] at 1693 cm^{-1}, as well as palladium carbonyl signals[17] at 2020 and 1961 cm^{-1}. Thus, the very hindered vinyl triflate does form an alkylpalladium(II) complex which is rapidly and quantitatively converted to the acylpalladium(II) complex by a migratory insertion of CO.

Under 3 atm of CO and in the presence of lithium chloride, equimolar amounts of vinyl triflate **14** and palladium catalyst **3**

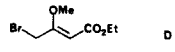
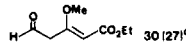
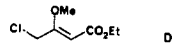
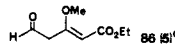
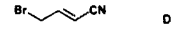
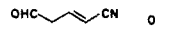
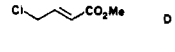
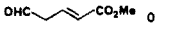
(14) (a) Kuivila, H. G. *Adv. Organomet. Chem.* **1963**, *1*, 47–87. (b) Leusink, A. J.; Budding, H. A.; Marsman, J. W. *J. Organomet. Chem.* **1967**, *9*, 285–294.

(15) Scott, W. J.; Crisp, G. T.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 4630–4632.

(16) (a) Booth, G.; Chatt, J. *J. Chem. Soc. A* **1966**, 634–638. (b) Fitton, P.; Johnson, M. P.; McKeon, J. A. *J. Chem. Soc., Chem. Commun.* **1968**, 6–7. (c) Kudo, K.; Sato, M.; Hidai, M.; Uchida, Y. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 2820–2822.

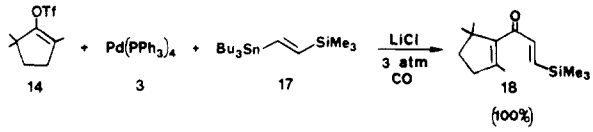
(17) Ono, E. H.; Nakagawa, K.; Moritani, I. *J. Organomet. Chem.* **1972**, *35*, 217–223.

Table V. Formylation of Allylic Halides

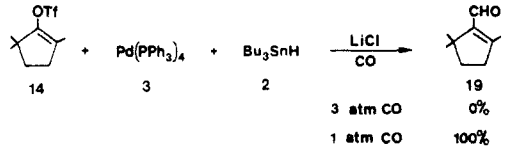
ENTRY	RX	Rxn Cond[b]	Products - % GC Yield (% isol Yield) RCHO	RH	RX
1		B	 14	c	0
2		B	 65 (31)[d]	23	0
3		D	 30 (27)[d]	45	0
4		D	 86 (5)[d]	14	0
5		D	 0	100	0
6		D	 0	100	0
7		D	 54 (54)[e]	46	0
8		D	 59 (59)[e]	41	0

[a] General conditions: 1–3 mmol of substrate in 3–10 mL of solvent, 50 °C, 3.5–4.0 mol % of $Pd(PPh_3)_4$, 0.5–1.5 mmol of ethylbenzene or toluene (as internal GC standard where appropriate), and 2.5–3.5-h addition of 1.1 equiv of Bu_3SnH diluted to 10 mL with the appropriate solvent. [b] Specific reaction conditions: A = Tol, 1 atm of CO; B = Tol, 3 atm of CO; C = THF, 1 atm of CO; D = THF, 3 atm of CO. [c] 54% yield of cyclohexene; 25% yield of 1,3-cyclohexadiene. [d] Isomerization occurred during workup; product isolated as the α,β-unsaurated aldehyde. [e] Product isolated and characterized as the 2,4-DNP derivative.

were allowed to react with tributyl((*E*)-2-(trimethylsilyl)vinyl)tin (**17**) to give ketone **18** in 100% yield. Thus, the desired oxidative

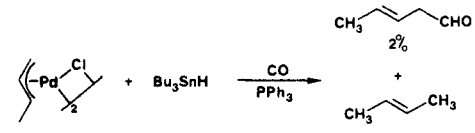


addition and CO insertion processes were able to occur at rates sufficient for product formation during a 2.5-h carbonylation reaction, in spite of the steric hindrance. Under the same conditions, treatment of the triflate with tributyltin hydride instead of the vinyl tin reagent gave no aldehyde (**19**). However, reducing



the pressure to 1 atm of CO resulted in a slow reaction which formed the desired product **19** in quantitative yield after 52 h. Therefore, the details of the mechanism of the hydride transfer apparently are different than those taking place in the transmetalation reaction of the vinyltin reagent **17**.

Formylation of Allylic Halides. Although allylic halides could be formylated to give β,γ-unsaturated aldehydes, double bond migration occurred during workup to yield the α,β-unsaturated aldehyde (Table V). The formylation of allylic halides resulted in moderate yields of aldehydes as a result of the competing reduction reaction. (π-Allyl)organotransition-metal complexes do not generally undergo migratory CO insertion readily.[18] When a preformed (π-allyl)palladium complex, crotylpalladium chloride dimer, was treated with tributyltin hydride under 3 atm of CO, only a trace of aldehyde was formed, and the remainder of the product was reduced material. Therefore, the yield of formylation

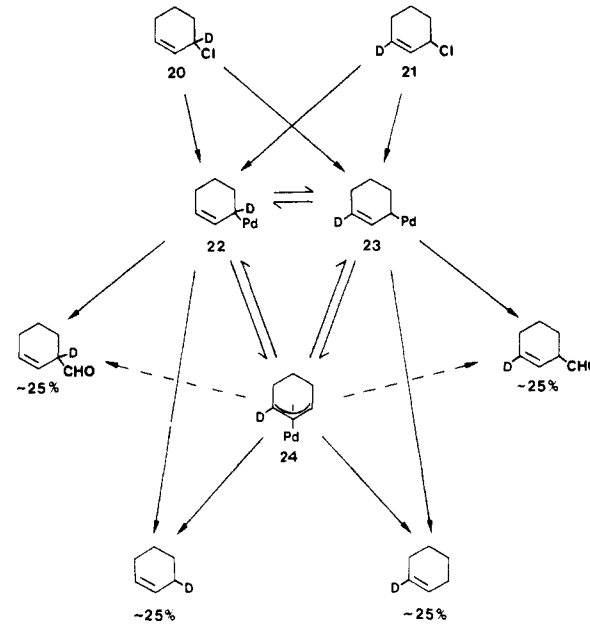


product would appear to be affected by the tendency of allylic halides to form (π-allyl)palladium complexes. Electron-poor allylic halides, which tend to readily form (π-allyl)palladium complexes,[19] were reduced quantitatively (entries 5, 6, Table V). However, increasing the electron density of the allylic system with an electron-donating methoxy substituent allowed the formylation to proceed (entries 3, 4, Table V).

The geometric integrity of allylic halide double bonds was maintained during the reactions of readily available and isomerically pure geranyl chloride[20] (entry 7, Table V) and neryl chloride[20] (entry 8, Table V). Because migration of the olefin of the β,γ-unsaturated aldehyde would result in loss of the stereochemical information, NMR and NOE experiments were conducted on the crude aldehydes, which indicated no olefin isomerization had occurred during the reaction. Conversion of the aldehyes to 2,4-DNP derivatives did not isomerize the double bonds (NOE), confirming that the geometry of the allylic double bond in the halide was maintained in the aldehyde and its 2,4-DNP derivatives.

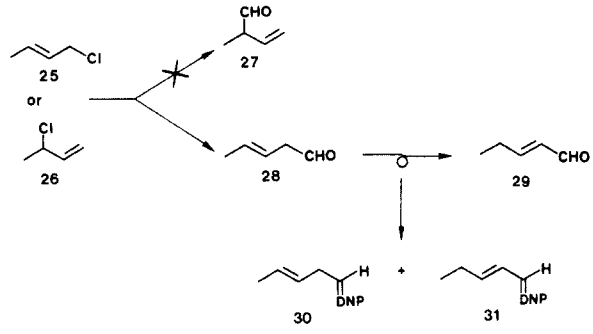
Formylation of specifically deuterated 3-chlorocyclohexenes **20** and **21** gave the same mixture (~50:50) of labeled cyclohexenyl aldehydes (Scheme II). The formylation reaction could proceed through a number of intermediate palladium complexes including rapidly equilibrating σ-complexes, **22** and **23**, and π-allyl complex **24**.[21] The aldehydes probably are formed via the σ-complexes, as the π-allyl complex **24** does not undergo CO insertion readily.[18] Nevertheless, both the formylated and reduced reaction products contained a statistical mixture of deuterium labeling indicating no regioselectivity with symmetrical allylic halides. However,

Scheme II



(18) (a) Heck, R. F.; Breslow, D. S. *J. Am. Chem. Soc.* **1961**, *83*, 1097–1102. (b) Powell, J.; Shaw, B. L. *J. Chem. Soc. A* **1967**, 1839–1851.
(19) (a) Parshall, G. W.; Wilkinson, G. *Inorg. Chem.* **1962**, *1*, 896–900. (b) Tsuji, J.; Imamura, S. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 197–201.
(20) Lissel, M.; Drechsler, K. *Synthesis* **1983**, 314–315.
(21) Sheffy, F. K.; Godschalz, J. P.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 4833–4840.

within an unsymmetrical allylic system, the formylation reaction occurred regioselectively at the less hindered position, regardless of which carbon possessed the leaving group. The formylation of 1-chloro-2-butene (**25**) and 3-chloro-1-butene (**26**) demonstrated this regioselectivity, as no 2-methyl-3-butenal (**27**) was observed.



Conclusion

A new synthetic method has been developed for the preparation of aldehydes from a wide variety of organic electrophiles. The palladium-catalyzed carbonylation reaction of the electrophile in the presence of tributyltin hydride as the hydride source yields aldehydes under mild conditions (50 °C, 1–3 atm of CO, and 2.5–3.5-h reaction times). The gentle nature of the reaction allows many functional groups to be tolerated, including alcohol, ester, aryl bromide and furan. Aryl iodides, benzyl halides, vinyl iodides, and vinyl triflates are generally formylated in high yields. Allylic halides tend to undergo the competing reduction reaction readily, thus giving aldehydes in moderate to low yields.

Experimental Section

Melting points were determined with a Mel-Temp capillary melting point apparatus and are uncorrected. ^{1}H NMR spectra were obtained on Varian EM-360 (60 MHz), JEOL FX-100 (100 MHz), IBM WP-200 (200 MHz), or IBM WP-270 (270 MHz) spectrometers, with tetramethylsilane (0.00 ppm) or chloroform (7.24 ppm) as internal standards. ^{2}H NMR spectra were obtained on an IBM-200 (30 MHz) spectrometer with deuteriochloroform (7.24 ppm) as an internal standard. ^{13}C NMR spectra were obtained on JEOL FX-100 (25 MHz), IBM WP-200 (50 MHz), or IBM WP-270 (68 MHz) spectrometers, with deuteriochloroform (77.0 ppm) as an internal standard. ^{31}P NMR spectra were obtained on an IBM-200 (81 MHz) spectrometer with 85% phosphoric acid (0.0 ppm) as external standard. Infrared spectra were obtained on a Beckman Model 4240 grating spectrophotometer (IR), a Perkin-Elmer Model 983 grating spectrophotometer (IR-PE983), or a Nicolet Model 60SX FTIR spectrophotometer (FTIR). NMR and IR spectra were compared to those of authentic samples when the compound was commercially available. Low-resolution mass spectra (LRMS) were obtained on a VG Micromass 16F spectrometer. High-resolution mass spectra (HRMS) were performed by the Midwest Center for Mass Spectrometry at the University of Nebraska. Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ. Gas chromatographic (GC) analyses were carried out on a Varian Model 3700 using an SE-30 packed glass capillary column (50 m × 0.25 mm i.d.). Peak areas were measured by electronic integration, and response factors of authentic samples vs. reference materials were calculated for determining GC yields.

Reactions conducted under 3 atm of CO utilized a 100-mL Fischer-Porter glass pressure reactor (Fischer-Porter Co.). Trialkyltin hydride solutions were dispensed from a 10-mL gas tight syringe (Hamilton) attached to a Sage Instrument Model 341A syringe pump. Radial chromatography was carried out with a Harrison Chromatotron (Harrison Research Co.).

Tetrahydrofuran (THF) was freshly distilled from sodium/benzophenone prior to use. Toluene was distilled from calcium hydride and stored over activated 4A sieves. The organic halides were either commercial products or prepared according to literature procedures. Tetrakis(triphenylphosphine)palladium(0) ($Pd(PPh_3)_4$),[22] bis(dibenzylideneacetone)palladium(0) ($Pd(dba)_2$),[23] tributyltin hydride (Bu_3SnH),[24] and trimethyltin hydride (Me_3SnH)[25] were prepared according to the published procedures.

General Procedure for Carbonylation Reactions. Method A: Toluene Solvent, 1 atm of Carbon Monoxide (15 psi). A three-neck flask was charged with 1–3 mmol of the organic halide, 3.5–4.0 mol % of $Pd(PPh_3)_4$, 0.5–1.5 mmol of ethylbenzene as an internal GC standard, if necessary, and 3–10 mL of toluene solvent. A double balloon pulled over a one-hole stopper was flushed 3 times with CO and connected to a condenser attached to the reaction flask. The system was flushed with a gentle steam of CO for 1 min and then placed in an oil bath at 50 °C. The trialkyltin hydride reagent, approximately a 10% excess, was measured by weight in a preweighed 10-mL gas tight syringe and then diluted with toluene to the 10-mL mark regardless of the millimole scale. This solution was added dropwise to the reaction mixture over 2.5 or 3.5 h by use of an automatic syringe pump. Upon completion of the addition, the reaction mixture was either analyzed by gas chromatography, or worked up, or both.

Method B: Toluene Solvent, 3 atm of Carbon Monoxide (45 psig). A pressure bottle (Fischer–Porter) charged as above with the organic halide, $Pd(PPh_3)_4$, ethylbenzene, and toluene was pressurized twice with CO to 45 psig and immediately vented without any stirring of the reaction mixture. Then, the pressure bottle was pressurized, and the solution was stirred vigorously. After 3–4 min, the CO was released and the vessel was flushed once again. Upon releasing the CO the final time, the needle of the 10-mL gas tight syringe, filled with the trialkyltin hydride solution, was inserted through a septum port into the vessel, and the syringe was attached to the syringe pump. With the carriage firmly against the plunger, the reaction vessel was refilled to 45 psig of CO. (**Caution**: The plunger will shoot from the syringe barrel with considerable force if it is not held in place.) With the aid of a number of rubber bands pulling on the carriage against the added back pressure, the trialkyltin hydride was added dropwise. Once the addition was complete, the reaction mixture was analyzed and worked up.

Method C: THF Solvent, 1 atm of Carbon Monoxide (15 psi). This method involved the same procedure as method A with THF used as the solvent.

Method D: THF Solvent, 3 atm of Carbon Monoxide (45 psig). This method involved the same procedure as method B with THF used as the solvent.

General Workup Procedures. Workup 1. The crude reaction mixture was diluted with 50 mL of ether, stirred vigorously with an equal volume of 50% saturated KF solution until no more flocculent, white precipitate formed (4–24 h), and was then filtered through a plug of glass wool. The organic layer was separated, washed with water and a saturated NaCl solution, and dried over either Na_2SO_4 or $MgSO_4$. The solution was concentrated, and the crude material was purified by chromatography.

Workup 2. The volatile materials were removed from the crude reaction mixture by a bulb-to-bulb vacuum transfer at 30–40 °C using a U-tube and trapped at liquid nitrogen temperature. The distilled solution was concentrated, and the crude material was purified by chromatography.

Workup 3. The crude reaction mixture was concentrated, and the resulting slurry was dissolved in an ether:hexane (1:1) mixture and filtered through a pad of Florisil. Concentration of the solution gave the crude product, which was purified by column chromatography.

Workup 4. The crude reaction mixture was washed with either a 10% ammonium hydroxide solution or water, followed by a saturated NaCl solution, and then dried. The mixture was then concentrated, and purified by chromatography.

Workup 5. The crude reaction mixture was added slowly to an acidic solution of 2,4-dinitrophenyl (2,4-DNP) hydrazine in ethanol and water, which resulted in the precipitation of the formylated product as the 2,4-DNP hydrazone derivative. Trace impurities were eliminated from the 2,4-DNP derivative by either recrystallization or chromatography.

4-Methoxybenzaldehyde (Entry 18, Table II). Method A; workup 1: Under 15 psi of CO, a 10-mL solution of 0.646 g (2.22 mmol) of Bu_3SnH in toluene was added over 2.5 h to a 50 °C solution of 0.467 g (2.00 mmol) of 4-iodoanisole, 0.0882 g (0.0763 mmol, 3.82 mol %) of $Pd(PPh_3)_4$, and 0.103 g (0.970 mmol) of ethylbenzene in 4 mL of toluene. GC analysis of the final reaction mixture indicated a 100% yield of 4-methoxybenzaldehyde. The reaction solution was taken up in 50 mL of ether and stirred with an equal volume of 50% saturated potassium fluoride solution for 24 h. The mixture was filtered through a plug of glass wool and the layers were separated. The organic layer was washed with water (20 mL) and a saturated sodium chloride solution (20 mL)

(22) Coulson, D. R. *Inorg. Synth.* **1972**, *13*, 121–124.
(23) (a) Takahashi, Y.; Ito, T.; Sakai, S.; Ishii, Y. *J. Chem. Soc., Chem. Commun.* **1970**, 1065–1066. (b) Moseley, K.; Maitlis, P. M. *J. Chem. Soc., Dalton Trans.* **1974**, 169–175.
(24) (a) Van der Kerk, G. J. M.; Noltes, J. G.; Luijten, J. G. A. *J. Appl. Chem.* **1957**, *7*, 366–369. (b) Hayashi, K.; Iyoda, J.; Shiihara, I. *J. Organomet. Chem.* **1967**, *10*, 81–94.
(25) Fish, R. H.; Kuivila, H. G.; Tyminski, L. J. *J. Am. Chem. Soc.* **1967**, *89*, 5861–5868.

and dried over sodium sulfate. Concentration of the solution under reduced pressure gave a crude material which was purified by flash column chromatography (silica gel; hexane, 10% ether/hexane, 50% ether/hexane) to afford 0.21 g (77% yield) of product as a pale, yellow oil: NMR ($CDCl_3$, 60 MHz) δ 3.82 (s, 3 H, OCH_3), 6.88 (d, J = 8 Hz, 2 H, Ar H), 7.70 (d, J = 8 Hz, 2 H, Ar H), 9.73 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 55.2, 113.9 (2 C), 129.5, 131.4 (2 C, 164.1, 190.1; IR ($CDCl_3$) 2740, 1700 cm^{-1}.

The following compounds were prepared in an analogous manner (method A, Tables II–V). Workup procedures were varied as noted.

2-Methylbenzaldehyde (Entry 17, Table II). Method A; workup 1: NMR ($CDCl_3$, 60 MHz) δ 2.58 (s, 3 H, CH_3), 6.84–7.78 (m, 4 H, Ar H), 10.10 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 19.5, 126.1, 131.5, 131.8, 133.3, 134.0, 140.3, 192.3; IR (neat) 2735, 1700 cm^{-1}.

3-(Hydroxymethyl)benzaldehyde (Entry 19, Table II).[26] Method A; workup 1; NMR ($CDCl_3$, 100 MHz) δ 4.21 (br s, 1 H, OH, eliminated by D_2O wash), 4.74 (s, 2 H, CH_2), 7.22–7.76 (m, 4 H, Ar H), 9.98 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 63.7, 127.3, 128.6, 128.7, 132.6, 136.0, 141.9, 192.4; IR (neat) 3995 (br), 2732, 1703 cm^{-1}.

2-(Hydroxymethyl)benzaldehyde (Entry 20, Table II).[27] Method A; workup 1; Product was isolated as a 3:1 isomer mixture of the ring-closed hemiacetal and the free aldehyde: NMR ($CDCl_3$, 60 MHz) δ 4.21 (t, J = 6 Hz, 0.25 H, OH), 4.73–5.47 (m, 2.75 H, CH_2, CH), 6.48 (d, J = 8 Hz, 0.75 H, OH), 7.05–7.68 (m, 4 H, Ar H), 10.02 (s, 0.25 H, CHO); IR ($CDCl_3$) 3395 (br), 2740, 1695 cm^{-1}.

1-Formylcyclohexene (Entry 1, Table IV).[28] Method A: workup 1; NMR ($CDCl_3$, 270 MHz) δ 1.56–1.63 (m, 4 H, CH_2CH_2), 2.12–2.15 (m, 2 H, CH_2), 2.26–2.30 (m, 2 H, CH_2), 6.74–6.77 (m, 1 H, =CH), 9.35 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 21.3 (2 C), 22.0, 26.4, 141.3, 151.1, 193.9; IR (neat) 2718, 1682, 1645 cm^{-1}.

4-Nitrobenzaldehyde (Entry 14, Table II). Method B; workup 1: Under 45 psig of CO, a 10-mL toluene solution of 0.660 g (2.27 mmol) of Bu_3SnH was added over 2.5 h to a solution of 0.506 g (2.03 mmol) of 1-iodo-4-nitrobenzene, 0.0896 g (0.0775 mmol, 3.81 mol %) of $Pd(PPh_3)_4$, and 0.109 g (1.03 mmol) of ethylbenzene in 10 mL of toluene at 50 °C. GC analysis of the final reaction mixture indicated a 38% yield of 4-nitrobenzaldehyde and a 62% yield of nitrobenzene. The reaction mixture was taken up in pentane, and the resulting precipitate was removed by filtration. Then, the crude product mixture was dissolved in 50 mL of ether and stirred with an equal volume of a saturated potassium fluoride solution for 4 h. The resulting mixture was filtered, and the ether layer was separated, washed with a saturated sodium chloride solution (25 mL), and dried over magnesium sulfate. The solution was concentrated under reduced pressure and the residue was purified by radial chromatography (4 mm silica gel plate; 20% ethyl acetate/hexane) to afford 0.062 g (20% yield) of the desired compound as a pale yellow solid: mp 104–105 °C [lit.[29] 106 °C]; NMR ($CDCl_3$, 60 MHz) δ 8.09 (d, J = 8.5 Hz, 2 H, Ar H), 8.42 (d, J = 8.5 Hz, 2 H, Ar H), 10.17 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 124.1 (2 C), 130.2 (2 C), 139.9, 150.9, 190.0; IR ($CDCl_3$) 2722, 1710, 1532, 1343 cm^{-1}.

The following compounds were prepared in an analogous manner (method B, Tables II–V). Workup procedures were varied as noted.

3-Formyl-2-cyclohexenone (Entry 7, Table IV).[30] Method B; workup 1: NMR ($CDCl_3$, 60 MHz) δ 1.78–2.67 (m, 6 H, CH_2), 6.40 (s, 1 H, =CH), 9.58 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 21.4, 21.6, 38.4, 138.7, 154.1, 194.0, 199.8; IR (neat) 2715, 1690, 1688 cm^{-1}.

(*E*)-2-Methyl-4-oxo-2-pentenal (Entry 9, Table IV). Method B; workup 2: NMR ($CDCl_3$, 270 MHz) δ 2.00 (d, J = 1.3 Hz, 3 H, CH_3), 2.33 (s, 3 H, CH_3), 6.73 (d, J = 1.4 Hz, 1 H, =CH), 9.45 (s, 1 H, CHO); NOE experiment (270 MHz, ^1H NMR). Irradiation at 6.73 ppm gave no enhancement at 2.00 ppm. ^{13}C NMR ($CDCl_3$, 68 MHz) δ 10.6, 31.4, 140.5, 146.9, 194.6, 198.4; IR ($CDCl_3$) 2700, 1694, 1688 cm^{-1}; LRMS, m/e (relative intensity) 112 (M^+, 21%); HRMS, calcd for $C_6H_8O_2$: 112.0522. Found: 112.0528.

1-Formylcyclohexene via 3-Formylcyclohexene (Entry 2, Table V) from 3-Chlorocyclohexene. Method B; workup 2: NMR ($CDCl_3$, 60 MHz) δ 1.17–2.08 (m, 6 H, CH_2), 2.30–2.55 (m, 2 H, CH_2), 6.72–6.81 (m, 1 H, =CH), 9.48 (s, 1 H, CHO). This compound was identical to that obtained from the formylation of cyclohexenyl iodide.

1-Formyl-2-methyl-1-cyclohexene (Entry 13, Table IV).[31] Method C; workup 2: Under 15 psi of CO, a 10-mL solution of 0.644 g (2.21 mmol) of Bu_3SnH in THF was added over 3.5 h to a 50 °C solution of 0.484 g (1.98 mmol) of 2-methyl-1-cyclohexenyl triflate, 0.086 g (0.074 mmol, 3.8 mol %) of $Pd(PPh_3)_4$, and 0.216 g (5.09 mmol) of lithium chloride in 8 mL of THF. GC analysis of the final reaction mixture indicated an 89% yield of aldehyde, an 8% yield of 1-methylcyclohexene, and a 3% yield of unreacted starting material. The volatile materials were collected by vacuum transfer. The solution was concentrated by distillation, and the resulting crude material was purified by radial chromatography (2 mm silica gel plate; pentane, 10% ether/pentane) to afford 0.13 g (53% yield) of the desired product[31] as a clear, colorless oil: NMR ($CDCl_3$, 270 MHz) δ 1.52–1.62 (m, 4 H, CH_2CH_2), 2.10–2.21 (m, 4 H, $CH_2C{=}CCH_2$), 2.13 (s, 3 H, CH_3), 10.15 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 18.2, 21.8, 22.1, 22.2, 34.2, 133.9, 155.3, 190.7; IR (neat) 2740, 1665, 1635, 1446, 1383, 1238 cm^{-1}; LRMS, m/e (relative intensity) 124 (M^+, 6%).

The following compounds were prepared in an analogous manner (method C, Tables II–V). Workup procedures were varied as noted.

4-Methylbenzaldehyde (Entry 15, Table II). Method C; workup 3: NMR ($CDCl_3$, 60 MHz) δ 2.36 (s, 3 H, CH_3), 7.20 (d, J = 8.5 Hz, 2 H, Ar H), 7.69 (d, J = 8.5 Hz, 2 H, Ar H), 9.90 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 21.5, 129.3 (4 C), 133.8, 145.0, 191.2; IR (neat) 2725, 1705 cm^{-1}.

1-Formylcyclopentene (Entry 3, Table IV).[32] Modified method C (Me_3SnH used as hydride source); workup 4 (H_2O): NMR ($CDCl_3$, 270 MHz) δ 1.94–1.99 (m, 2 H, CH_2), 2.02–2.56 (m, 2 H, CH_2), 2.57–2.65 (m, 2 H, CH_2), 6.87–6.90 (m, 1 H, =CH), 9.79 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 22.8, 28.2, 33.4, 147.8, 152.5, 189.4; IR ($CDCl_3$) 2700, 1672, 1607 cm^{-1}; LRMS; m/e (relative intensity) 96 (M^+, 56%).

1-Formyl-2,5,5-trimethylcyclopentene (Entry 15, Table IV).[33] Method C; workup 2: (crude aldehyde) NMR ($CDCl_3$, 270 MHz) δ 1.67 (t, J = 7.3 Hz, 2 H, CH_2), 2.10 (s, 3 H, CH_3), 2.45 (t, J = 7.2 Hz, 2 H, CH_2), 9.98 (s, 1 H, CHO); crude ^{13}C NMR ($CDCl_3$, 68 MHz) δ 14.2, 26.8 (2 C), 31.5, 37.3, 39.1, 188.1; IR ($CDCl_3$) 2718, 1667, 1624 cm^{-1}; GC/LRMS, m/e (relative intensity) 138 (M^+, 2%).

In a separate procedure, method C; workup 5: (2,4-DNP) mp 206–207 °C [lit.[33] 207–209 °C]; NMR ($CDCl_3$, 270 MHz) δ 1.35 (s, 6 H, CH_3), 1.77 (t, J = 7.4 Hz, 2 H, CH_2), 1.95 (s, 3 H, CH_3), 2.45 (t, J = 7.3 Hz, 2 H, CH_2), 7.86 (d, J = 9.6 Hz, 1 H, Ar H), 7.98 (s, 1 H, CH=N), 8.31 (dd, J = 2.3, 9.8 Hz, 1 H, Ar H), 9.12 (d, J = 2.5 Hz, 1 H, Ar H), 11.1 (s, 1 H, NH); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 15.0, 27.3 (2 C), 37.0, 39.7, 46.8, 116.5, 123.5, 129.1, 129.9, 137.8, 138.6, 144.5, 144.9, 150.4; IR ($CDCl_3$) 3294, 1618, 1591, 1518, 1506, 1420, 1330 cm^{-1}.

4,8-Dimethyl-3(*E*),7-nonadienal (Entry 7, Table V). Method D; workup 5: Under 45 psi of CO, a 10-mL THF solution of 0.961 g (3.30 mmol) of Bu_3SnH was added over 4 h to a 50 °C solution of 0.526 g (3.04 mmol) of geranyl chloride and 0.132 g (0.114 mmol, 3.75 mol %) of $Pd(PPh_3)_4$ in 10 mL of THF. Upon completion of the addition, the crude mixture was concentrated under reduced pressure. Analysis of the resulting residue by NMR indicated a 54% yield of the desired aldehyde[34] and a 46% yield of the reduced material: Crude NMR ($CDCl_3$, 270 MHz) δ 1.60 (s, CH_3), 1.64 (s, CH_3), 1.68 (s, CH_3), 2.05–2.16 (m, CH_2), 3.13 (dm, J = 7 Hz, CH_2), 5.04–5.15 (m, =CH), 5.31 (tm, J = 7 Hz, =CH), 9.62 (t, J = 2 Hz, CHO); decoupling experiment (270 MHz, ^1H NMR). Triplet at 9.62 ppm (CHO) collapsed to a singlet upon irradiation at 3.13 ppm (CH_2). NOE experiment (270 MHz, ^1H NMR): Irradiation at 2.10 ppm (CH_2) enhanced the peak at 5.31 ppm by 16%; irradiation at 1.68 ppm (CH_3) gave no enhancement at 5.31 ppm. Crude IR (neat) 2719, 1725 cm^{-1}.

The aldehyde product was trapped as a 2,4-dinitrophenyl hydrazone derivative, since isolation methods previously used had failed. The crude material was taken up in 10 mL of 95% ethanol and added to a 2,4-dinitrophenylhydrazine solution [0.896 g (4.53 mmol) in 15 mL of 95% ethanol, 6 mL of water and 3 mL of concentrated sulfuric acid], which immediately formed a yellow precipitate. The mixture was stirred overnight at room temperature, cooled to −20 °C for several hours, and filtered to afford 0.56 g (100% yield based on crude aldehyde) of the desired 2,4-DNP compound as a dull orange solid; mp 75–85 °C. NMR analysis of the crude derivative showed no absorption at 1.78 ppm indicating that none of the 3*Z*-isomer was formed, and NOE experiments indicated that the product was the 3*E*-isomer. NOE experiment (270 MHz, ^1H NMR): Irradiation at 2.08 ppm (CH_2) enhanced the peak at 5.25 ppm by 14%; irradiation at 1.70 ppm (CH_3) gave no enhancement at 5.25 ppm. Examination of the mother liquor by NMR spectroscopy

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indicated no aldehyde or 2,4-DNP adduct remained in solution.

Purification of a portion of the material by recrystallization (ethanol) followed by radial chromatography (2 mm silica gel plate; 10% ethyl acetate/hexane) gave an analytically pure sample as bright orange crystals: mp 87–89 °C; NMR ($CDCl_3$, 270 MHz) δ 1.62 (s, 3 H, CH_3), 1.69 (s, 3 H, CH_3), 1.71 (s, 3 H, CH_3), 2.02–2.14 (m, 4 H, CH_2CH_2), 3.15 (dd, J = 5.4, 7.3 Hz, 2 H, CH_2), 5.08–5.12 (m, 1 H, =CH), 5.26 (tm, J = 7.2 Hz, 1 H, =CH), 7.43 (t, J = 5.4 Hz, 1 H, CH=N), 7.94 (d, J = 9.5 Hz, 1 H, Ar H), 8.29 (dd, J = 2.5, 9.6 Hz, 1 H, Ar H), 9.11 (d, J = 2.5 Hz, 1 H, Ar H), 11.02 (br s, 1 H, NH); NOE experiment (270 MHz, ^{1}H NMR). Irradiation at 2.10 ppm (CH_2) enhanced the peak at 5.26 ppm by 16%, irradiation at 1.71 ppm (CH_3) gave no enhancement at 5.26 ppm. ^{13}C NMR ($CDCl_3$, 68 MHz) δ 16.4, 17.6, 25.6, 26.6, 31.6, 39.7, 116.5, 123.4, 123.9, 129.1, 129.9, 131.7, 138.7, 140.1, 145.2, 150.8, 150.9; IR ($CDCl_3$) 3300, 1642, 1593, 1518, 1333, 1307 cm^{-1}; LRMS, m/e (relative intensity) 346 (M^+, 1%). Anal. Calcd for $C_{17}H_{22}N_4O_4$: C, 58.94; H, 6.41; N, 16.18. Found: C, 59.02; H, 6.52; N, 16.05.

The following compounds were prepared in an analogous manner (method D, Tables II–V). Workup procedures were varied as noted.

4,8-Dimethyl-3(Z),7-nonadienal (Entry 8, Table V). Method D; workup 5: (crude aldehyde) NMR ($CDCl_3$, 270 MHz) δ 1.62 (s, CH_3), 1.68 (s, CH_3), 1.75 (s, CH_3), 2.02–2.15 (m, CH_2), 3.13 (dm, J = 7 Hz, CH_2), 5.05–5.14 (m, =CH), 5.31 (tm, J = 7 Hz, =CH), 9.60 (t, J = 2 Hz, CHO); decoupling experiment (270 MHz, ^{1}H NMR). Triplet at 9.60 ppm (CHO) collapsed to a singlet upon irradiation at 3.13 ppm (CH_2). NOE experiment (270 MHz, ^{1}H NMR): Irradiation at 1.75 ppm (CH_3) enhanced the peak at 5.31 ppm by 10%; irradiation at 2.08 ppm (CH_2) gave no enhancement at 5.31 ppm. IR (neat) 2718, 1720 cm^{-1}.

Crude 2,4-DNP: mp 61–64 °C. NMR analysis of the crude derivative showed no adsorption at 1.71 ppm, indicating that none of the 3E-isomer was formed, and NOE experiments indicated that the product was the 3Z-isomer. NOE experiment (270 MHz, ^{1}H NMR): Irradiation at 1.76 ppm (CH_3) enhanced the peak at 5.25 ppm by 15%; irradiation at 2.10 ppm (CH_2) gave no enhancement at 5.25 ppm.

Purified 2,4-DNP: mp 65–67 °C; NMR ($CDCl_3$, 270 MHz) δ 1.61 (s, 3 H, CH_3), 1.69 (s, 3 H, CH_3), 1.78 (s, 3 H, CH_3), 1.99–2.19 (m, 4 H, CH_2CH_2), 3.14 (dd, J = 5.4, 7.3 Hz, 2 H, CH_2), 5.10–5.12 (m, 1 H, =CH), 5.26 (tm, J = 7.4 Hz, 1 H, =CH), 7.44 (t, J = 5.5 Hz, 1 H, CH=N), 7.95 (d, J = 9.5 Hz, 1 H, Ar H), 8.29 (dd, J = 2.2, 9.7 Hz, 1 H, Ar H), 9.10 (d, J = 2.4 Hz, 1 H, ArH), 11.01 (br s, 1 H, NH); NOE experiment (270 MHz, ^{1}H NMR). Irradiation at 1.78 ppm (CH_3) enhanced the peak at 5.26 ppm by 20%; irradiation at 2.12 ppm (CH_2) gave no enhancement at 5.26 ppm; ^{13}C NMR ($CDCl_3$, 68 MHz) δ 17.5, 23.3, 25.5, 26.4, 31.5, 32.1, 116.5, 117.3, 123.2, 123.8, 129.7, 131.9, 137.9, 140.0, 145.1, 149.6, 151.1; IR ($CDCl_3$) 3300, 1640, 1592, 1507, 1423, 1332, 1308 cm^{-1}; LRMS, m/e (relative intensity) 346 (M^+, 2%). Anal. Calcd for $C_{17}H_{22}N_4O_4$: C, 58.94; H, 6.41; N, 16.18. Found: C, 58.86; H, 6.28; N, 16.11.

4-Bromobenzaldehyde (Entry 3, Table II). Method D; workup 1: mp 50–54 °C [lit.[35] 57 °C]; NMR ($CDCl_3$, 100 MHz) δ 7.73 (s, 4 H, Ar H), 10.02 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 129.2, 130.5 (2 C), 131.9 (2 C), 134.7, 190.3; IR ($CDCl_3$) 2760, 1687 cm^{-1}.

3-Chlorobenzaldehyde (Entry 4, Table II).[36] Method D; workup 3: NMR ($CDCl_3$, 270 MHz) δ 7.48 (dd, J = 7.6, 7.8 Hz, 1 H, Ar H), 7.59 (dm, J = 7.8 Hz, 1 H, Ar H), 7.77 (dm, J = 7.6 Hz, 1 H, Ar H), 7.83–7.85 (m, 1 H, Ar H), 9.98 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 127.8, 129.2, 130.3, 134.2, 135.5, 138.0, 190.5; IR (neat) 2720, 1700 cm^{-1}.

4-Chlorobenzaldehyde (Entry 5, Table II). Method D, workup 2: mp 44–45 °C [lit.[36] 47 °C]; NMR ($CDCl_3$, 270 MHz) δ 7.52 (dm, J = 8.4 Hz, 2 H, Ar H), 7.83 (dm, J = 8.5 Hz, 2 H, Ar H), 9.99 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 129.5, 130.9 (2 C), 135.0 (2 C), 141.0, 190.5; IR (neat) 2725, 1704 cm^{-1}.

Methyl 4-Formylbenzoate (Entry 7, Table II). Method D; workup 3: mp 61–62 °C [lit.[37] 63 °C]; NMR ($CDCl_3$, 270 MHz) δ 3.97 (s, 3 H, CH_3), 7.96 (dm, J = 8.3 Hz, 2 H, Ar H), 8.20 (dm, J = 8.3 Hz, 2 H, Ar H), 10.11 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 52.3, 129.3 (2 C), 130.0 (2 C), 134.9, 139.1, 165.8, 191.2; IR ($CDCl_3$) 2730, 1728, 1709 cm^{-1}.

Methyl 3-Formylbenzoate (Entry 8, Table II). Method D; workup 3: mp 51–52 °C [lit.[38] 52–53 °C]; NMR ($CDCl_3$, 270 MHz) δ 3.97 (s, 3 H, CH_3), 7.64 (dd, J = 7.7, 7.6 Hz, 1 H, Ar H), 8.10 (dm, J = 7.7 Hz, 1 H, Ar H), 8.31 (dm, J = 7.7 Hz, 1 H, Ar H), 8.53–8.56 (m, 1 H, Ar H), 10.09 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 52.4, 129.2, 131.2, 131.4, 133.0, 135.1, 136.7, 165.9, 191.1; IR ($CDCl_3$) 2720, 1725, 1705 cm^{-1}.

Methyl 2-Formylbenzoate (Entry 9, Table II).[39] Method D; workup 3: NMR ($CDCl_3$, 270 MHz) δ 3.97 (s, 3 H, CH_3), 7.63–7.66 (m, 2 H, Ar H), 7.91–7.98 (m, 2 H, Ar H), 10.61 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 52.5, 128.3, 130.2, 132.0, 132.2, 132.7, 137.1, 166.6, 191.7; IR (neat) 2758, 1750, 1702 cm^{-1}.

4-(Trifluoromethyl)benzaldehyde (Entry 10, Table II). Method D; workup 3: NMR ($CDCl_3$, 270 MHz) δ 7.80 (d, J = 8.1 Hz, 2 H, Ar H), 8.01 (d, J = 8.0 Hz, 2 H, Ar H), 10.1 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 123.5 (q, J = 272.6 Hz, CF_3), 126.0 (2 C), 129.7 (2 C), 135.6 (q, J = 32.8 Hz), 138.9, 190.6; IR (neat) 2730, 1718 cm^{-1}.

***o*-Formylbenzyl Tetrahydropyranyl Ether (Entry 21, Table II).** Method D; workup 1: NMR ($CDCl_3$, 270 MHz) δ 1.52–1.90 (m, 6 H, CH_2), 3.50–3.62 (m, 1 H, OCHC), 3.85–3.93 (m, 1 H, OCHC), 4.77 (t, J = 3.4 Hz, 1 H, OCHO), 4.94 (d, J = 14.2 Hz, 1 H, Ar CH), 5.19 (d, J = 14.2 Hz, 1 H, Ar CH), 7.46 (t, J = 7.4 Hz, 1 H, Ar H), 7.59 (t, J = 7.3 Hz, 1 H, Ar H), 7.67 (d, J = 7.4 Hz, 1 H, Ar H), 7.86 (d, J = 7.5 Hz, 1 H, Ar H), 10.26 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 19.4, 25.3, 30.5, 62.3, 66.2, 98.4, 127.6, 128.4, 131.7, 133.6 (2 C), 140.8, 192.4; IR (neat) 2716, 1698, 1135, 1121, 1077, 1058, 1031 cm^{-1}; LRMS (70 eV), m/e (relative intensity) 136 ($M^+ - C_5H_8$, 4%); LRMS (CI), m/e (relative intensity) 221 ($M^+ + 1$, 1%); HRMS, calcd for $C_{13}H_{16}O_3$: 220.1100. Found: 220.1092.

3-Furfural (Entry 22, Table II).[40] Method D; modified workup 2 (final purification was a bulb-to-bulb distillation): bp 25 °C (0.05 mmHg); NMR ($CDCl_3$, 270 MHz) δ 6.80 (br d, J = 1.9 Hz, 1 H, =CH), 7.51 (dd, J = 1.4, 1.9 Hz, 1 H, =C—O), 8.12 (dd, J = 1.4, 0.8 Hz, 1 H, =CHO), 9.96 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 106.9, 128.8, 144.7, 150.8, 183.8; IR (neat) 2728, 1692, 1568, 1512, 1152, 1065 cm^{-1}; LRMS, m/e (relative intensity) 96 (M^+, 80%).

Phenylacetaldehyde (Entry 3, Table III). Method D; workup 5: (2,4-DNP derivative) mp 120–122 °C [lit.[35] 121 °C]; NMR ($CDCl_3$, 270 MHz) δ 3.76 (d, J = 5.8 Hz, 2 H, CH_2), 7.25–7.40 (m, 5 H, Ar H), 7.60 (t, J = 5.8 Hz, 1 H, =CH), 7.97 (d, J = 9.6 Hz, 1 H, Ar H), 8.33 (dd, J = 2.5, 9.6 Hz, 1 H, Ar H), 9.15 (d, J = 2.5 Hz, 1 H, Ar H), 11.06 (br s, 1 H, NH); IR ($CDCl_3$) 3304, 1622, 1520, 1337 cm^{-1}.

3-Furfurylaldehyde (Entry 4, Table III). Method D; modified workup 2 (final purification was a bulb-to-bulb distillation): bp 25 °C (0.4 mmHg); NMR ($CDCl_3$, 270 MHz) δ 3.52–3.54 (m, 2 H, CH_2), 6.33 (s, 1 H, =CH), 7.40–7.44 (m, 2 H, =CHOCH=), 9.71 (t, J = 2.0 Hz, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 39.7, 111.2, 115.2, 140.6, 143.3, 198.3; IR (neat) 2730, 1732, 1580, 1505, 1383, 1158, 1080, 1022 cm^{-1}; LRMS, m/e (relative intensity) 110 (M^+, 36%); HRMS, calcd for $C_6H_6O_2$: 110.0368. Found: 110.0368.

4-*tert*-Butyl-1-formylcyclohexene (Entry 2, Table IV)[35] from 4-*tert*-Butyl-1-iodocyclohexene. Method D; workup 4 (NH_4OH): NMR ($CDCl_3$, 270 MHz) δ 0.91 (s, 9 H, CH_3) 1.07–1.36 (m, 2 H, CH_2), 1.91–2.12 (m, 3 H, CH_2, CH), 2.36–2.53 (m, 2 H, CH_2), 6.82 (m, 1 H, =CH), 9.43 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 22.5, 22.8, 26.9 (3 C), 28.0, 31.9, 44.0, 141.2, 150.3, 192.6; IR (neat) 2705, 1688, 1650 cm^{-1}.

***trans*-2-Heptenal (Entry 4, Table IV)[41] from *trans*-1-Iodo-1-hexene.** Method D, workup 2: NMR ($CDCl_3$, 270 MHz) δ 0.86 (t, J = 7.2 Hz, 3 H, CH_3), 1.23–1.34 (m, 2 H, CH_2), 1.37–1.55 (m, 2 H, CH_2), 2.20–2.35 (m, 2 H, $=CCH_2$), 6.03 (ddt, J = 8.0, 15.6, 1.4 Hz, 1 H, =CH—CO), 6.79 (dt, J = 15.5, 6.8 Hz, 1 H, =CH), 9.43 (d, J = 7.9 Hz, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 13.5, 22.1, 30.0, 32.2, 133.1, 157.7, 193.2; IR (neat) 2733, 1698, 1660 cm^{-1}.

***trans*-2-Heptenal (Entry 5, Table IV) from *cis*-1-Iodo-1-hexene.** Method D; workup 2: GC analysis of the final reaction mixture indicated an 85:15 cis to trans isomer ratio. All methods of isolation (flash distillation, chromatography, or vacuum transfer) resulted in quantitative isomerization of the cis isomer to the trans isomer as determined by both GC and NMR analyses. Spectra for isolated trans product matched those reported above.

4-*tert*-Butyl-1-formylcyclohexene (Entry 11, Table IV) from 4-*tert*-Butyl-1-cyclohexenyl Triflate. Method D; workup 4 (NH_4OH): This compound was identical to that obtained from the formylation of the corresponding 4-*tert*-Butyl-1-iodocyclohexene.

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1-Formyl-6-methyl-1-cyclohexene (Entry 12, Table IV).[42] Method D; workup 2: NMR ($CDCl_3$, 270 MHz) δ 1.08 (d, J = 6.9 Hz, 3 H, CH_3), 1.50–1.75 (m, 4 H), 2.19–2.34 (m, 2 H), 2.65–2.70 (m, 1 H), 6.75 (br t, J = 3.8 Hz, 1 H, =CH), 9.37 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 18.1, 19.4, 26.1, 26.7, 29.5, 146.5, 150.7, 193.3; IR (neat) 2704, 1688, 1680 cm^{-1}; LRMS, m/e (relative intensity) 124 (M^+, 10%).

Ethyl 3-Methoxy-5-oxo-3-pentenoate (Entry 3, Table V) via Ethyl 3-Methoxy-5-oxo-2-pentenoate from Ethyl 4-Bromo-3-methoxy-2-butenoate. Method D; workup 1: NMR ($CDCl_3$, 100 MHz) δ 1.27 (t, J = 7.2 Hz, 3 H, CCH_3), 3.65 (s, 2 H, $=CCH_2$), 3.74 (s, 3 H, OCH_3), 4.19 (q, J = 7.1 Hz, 2 H, OCH_2), 5.53 (d, J = 7.0 Hz, 1 H, =CH), 9.74 (d, J = 7.0 Hz, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 14.1, 37.9, 56.3, 61.5, 105.4, 167.7, 171.0, 189.2; IR (neat) 2740, 1746, 1668, 1623 cm^{-1}; LRMS, m/e (relative intensity) 172 (M^+, 2%); HRMS (CI), calcd for $C_8H_{13}O_4$: 173.0816. Found: 173.0818.

Ethyl 3-Methoxy-5-oxo-3-pentenoate (Entry 4, Table V) via Ethyl 3-Methoxy-5-oxo-2-pentenoate from Ethyl 4-Chloro-3-methoxy-2-butenoate. Method D; workup 1: Spectra matched those reported above.

Carbonylation of 1,4-Diiodobenzene. One Equivalent of Bu_3SnH. Under 15 psi of CO, a 10-mL toluene solution of 0.636 g (2.19 mmol) of Bu_3SnH was added over 2.5 h to a 50 °C solution of 0.659 g (2.00 mmol) of 1,4-diiodobenzene, 0.0872 g (0.0754 mmol, 3.78 mol %) of $Pd(PPh_3)_4$, and 0.100 g (0.947 mmol) of ethylbenzene in 6 mL of toluene. GC analysis of the final reaction mixture indicated a 17% yield of benzaldehyde, a 25% yield of iodobenzene, a 2% yield of benzene, and a 50% yield of unreacted starting material. No product isolation was carried out.

Two Equivalents of Bu_3SnH. The above procedure was repeated using 2 equiv of Bu_3SnH/equiv of diiodide. The crude reaction mixture contained a 58% yield of benzaldehyde and a 39% yield of benzene by GC analysis. No product isolation was carried out.

3-Tributylstannyl-2-heptenal and 3-Butyl-2-nonen-4-ynal. Method D; workup 1: Under 45 psig of CO, a solution of 0.969 g (3.33 mmol) of Bu_3SnH was added as a 10-mL THF solution over 2.5 h to a 50 °C solution of 0.627 g (3.01 mmol) of 1-iodo-1-hexyne and 0.132 g (0.114 mmol, 3.80 mol %) of $Pd(PPh_3)_4$ in 10 mL of THF. Upon completion of the addition, the reaction mixture was cooled and concentrated under reduced pressure. The residue was taken up in 80 mL of ether and stirred with an equal volume of a 50% saturated potassium fluoride solution for 2 h. The mixture was filtered through a plug of glass wool, the resulting layers were separated, and the organic solution was stirred with a second potassium fluoride solution. The organic layer was separated, washed with water (2 × 20 mL) and a saturated sodium chloride solution (20 mL), and dried over sodium sulfate. Removal of the solvent under reduced pressure gave 1.21 g of a dark orange oil. Purification by radial chromatography (4 mm silica gel plate; 5% ether/hexane) gave 0.307 g (26% yield) of 3-(tributylstannyl)-2-heptenal followed by 0.111 g (38% yield) of 3-butyl-2-nonen-4-ynal, both as pale yellow oils.

3-(Tributylstannyl)-2-heptenal: NMR ($CDCl_3$, 270 MHz) δ 0.80–1.10 (m, 2 OH), 1.21–1.41 (m, 1 OH), 1.45–1.65 (m, 4 H), 2.23–2.31 (m, 2 H, CH_2C=), 7.26 (s, 1 H, =CH), 9.42 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 10.5, 13.5, 23.1, 27.3, 29.1, 31.4, 31.6, 32.1, 157.1, 159.5, 193.7; IR ($CDCl_3$) 2688, 1688, 1581 cm^{-1}; LRMS, m/e (relative intensity) 345 ($M^+ - C_4H_8$, 100%), 289 ($M^+ - 2[C_4H_8]$, 86%), 233 ($M^+ - 3[C_4H_8]$, 71%); Anal. Calcd. for $C_{19}H_{38}OSn$: C, 56.88; H, 9.55. Found: C, 56.63; H, 9.68.

3-Butylnon-2-en-4-ynal: NMR ($CDCl_3$, 270 MHz) δ 0.91 (t, J = 7.1 Hz, 3 H, CH_3), 0.94 (t, J = 7.2 Hz, 3 H, CH_3), 1.28–1.61 (m, 8 H), 2.38–2.51 (m, 4 H, CH_2C=, CH_2C–), 6.32 (t, J = 2.2 Hz, 1 H, =CH), 9.41 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 13.4, 13.7, 19.8, 22.0, 22.7, 25.9, 30.3, 30.5, 77.3, 109.2, 130.0, 151.9, 194.0; IR ($CDCl_3$) 2718, 2205, 1682, 1603 cm^{-1}; LRMS, m/e (relative intensity) 192 (M^+, 15%); Anal. Calcd. for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 80.94; H, 10.24.

Stoichiometric Palladium Reaction: Examination for an Acylpalladium Complex via IR and ^{31}P Analyses. IR Analysis/1 atm of CO. A 3-mL THF solution of 82 mg (0.32 mmol) of 2,5,5-trimethyl-1-cyclopentenyl triflate, 366 mg (0.32 mmol) of $Pd(PPh_3)_4$, and 35 mg (0.83 mmol) of lithium chloride was stirred under 15 psi of CO at 50 °C for 2 h. The mixture was then cooled, a portion of the mixture was syringed into an airless IR cell, and the IR spectrum was taken. The cell was then flushed and used to take a spectrum of neat THF, which was computationally subtracted from the spectrum of the solution. The difference IR spectrum suggested the presence of an acylpalladium species: IR-PE983 2017, 1961, 1694, 1585, 1571, 1480, 1434, 1310 cm^{-1}.

In a separate experiment, a 50 °C solution of 54.2 mg (0.210 mmol) of 2,5,5-trimethyl-1-cyclopentenyl triflate, 239 mg (0.207 mmol) of $Pd(PPh_3)_4$, and 19.2 mg (0.453 mmol) of lithium chloride in 15 mL of THF was prepared under argon. The solution was examined by FTIR after 1 h, and the spectrum of the starting vinyl triflate solution (17.3 mg [0.0671 mmol] in 5 mL of THF) was computationally subtracted: FTIR 1585, 1572, 1481, 1434, 1311 cm^{-1}. The vessel was flushed gently with CO for 1 min and pressurized for 4 min with a CO balloon (15 psi). The solution was reexamined by FTIR, and again the spectrum of the starting vinyl triflate solution was subtracted: FTIR 2020, 1961, 1693, 1585, 1573, 1482, 1435, 1310 cm^{-1}. The mixture was stirred under 15 psi of CO for 2 h, and FTIR analysis showed no change from the product mixture obtained after 5 min of CO reaction.

IR Analysis/3 atm of CO. The first procedure above was repeated with the solution stirred under 45 psig of CO for 1 h. The mixture was cooled, the CO was slowly released, and a sample of the solution was examined by IR. The subtracted IR spectrum matched the spectra observed for the 15 psi CO experiment: IR-PE983 2017, 1959, 1695, 1585, 1572, 1479, 1430, 1307 cm^{-1}.

^{31}P NMR Analysis/1 atm of CO. In a 10-mm NMR tube was prepared a solution of 94 mg (0.081 mmol) of $Pd(PPh_3)_4$ and 12 mg (0.28 mmol) of lithium chloride in 2.5 mL of THF with 0.5 mL of benzene-d_6. The solution was warmed to 50 °C for 30 min and examined by ^{31}P NMR: ^{31}P NMR (THF/C_6D_6, 81 MHz) δ 25.9 (s), 23.6 (s), –4.6 (s). Then, 23 mg (0.089 mmol) of 2,5,5-trimethyl-1-cyclopentenyl triflate was added to the mixture, heated for 1 h at 50 °C, and reexamined: ^{31}P NMR (THF/C_6D_6, 81 MHz) δ 27.1 (s), 23.7 (s), 23.3 (s), –4.7 (s). CO was gently bubbled through this solution for 5 min at 50 °C, and the sample was reexamined: ^{31}P NMR (THF/C_6D_6, 81 MHz) δ 26.1 (s), 23.8 (s), 15.1 (s), 15.1 (s), –4.2 (s). Bubbling CO through the solution for 30 min did not cause any peaks to shift; however, the intensity of the peak at 15.1 ppm decreased. Addition of triphenylphosphine oxide to the sample increased the peak at 26.1 ppm, and added triphenylphosphine increased the peak at –4.2 ppm.

Stoichiometric Palladium Reaction: Carbonylation of 2,5,5-Trimethyl-1-cyclopentenyl Triflate with Tributyl((*E*)-2-(trimethylsilyl)-vinyl)tin. Under 45 psig of CO, a solution of 0.383 g (1.48 mmol) of 2,5,5-trimethyl-1-cyclopentenyl triflate, 1.74 g (1.50 mmol) of $Pd(PPh_3)_4$, and 0.143 g (3.37 mmol) of lithium chloride was prepared in 15 mL of THF. As the solids dissolved, a drop in CO pressure was observed, and additional CO was added. Then, 0.639 g (1.64 mmol) of tributyl-((*E*)-2-(trimethyl-silyl)vinyl)tin was added to the reaction mixture as a 10-mL THF solution over 3.5 h at 55 °C. Upon completion of the addition, the mixture was concentrated under reduced pressure. The resulting solid was slurried in hexane and filtered through a plug of Florisil with the aid of a small volume of a 5% ethyl acetate/hexane solution. The solution was concentrated under reduced pressure, and the residue was purified by radial chromatography (2 mm silica gel plate; pentane, 5% ethyl acetate/hexane) to give 0.349 g (100% yield) of the ketone[9c] as a white solid: mp 78–79 °C; NMR ($CDCl_3$, 270 MHz) δ 0.07 (s, 9 H, $SiCH_3$), 1.13 (s, 6 H, CH_3), 1.73 (s, 3 H, CH_3), 1.81 (t, J = 7 Hz, 2 H, CH_2), 2.30 (t, J = 7 Hz, 2 H, CH_2), 6.61 (d, J = 19 Hz, 1 H, =CH), 6.90 (d, J = 19 Hz, 1 H, =CH); ^{13}C NMR ($CDCl_3$, 68 MHz) δ –1.9 (3 C), 16.7, 27.2 (2 C), 29.7, 36.9, 40.3, 144.1, 144.5, 145.1, 146.7, 195.2; IR ($CDCl_3$) 1650, 1585, 1485, 1240, 1272, 1253 cm^{-1}.

Stoichiometric Palladium Reaction: Carbonylation of 2,5,5-Trimethyl-1-cyclopentenyl Triflate with Tributyltin Hydride. One Atmosphere of CO. A mixture of 0.258 g (1.00 mmol) of 2,5,5-trimethyl-1-cyclopentenyl triflate, 1.16 g (1.00 mmol) of $Pd(PPh_3)_4$, and 0.085 g (2.0 mmol) of lithium chloride was taken up in 15 mL of THF to give a thick bright yellow slurry. Under 15 psi of CO, the mixture was heated to 50 °C and the slurry dissolved to give a clear orange solution. The solution was stirred for 15 min and to it was added a 10-mL THF solution of 0.324 g (1.11 mmol) of Bu_3SnH over 3.5 h. Upon completion of the addition, GC analysis indicated a 6% yield of aldehyde and no unreacted vinyl triflate. The mixture was allowed to stir for an additional 3 h, and GC analysis of the mixture indicated an 11% yield of aldehyde. The reaction was monitored periodically by GC analysis, which showed a gradual increase in the yield of aldehyde. During the additional reaction time, the reaction mixture gradually precipitated a dull yellow solid. After 52 h, a quantitative yield of 1-formyl-2,5,5-trimethylcyclopentene was observed with no reduced product formed.

Three Atmospheres of CO. The above procedure was repeated under 45 psig of CO. The thick, bright yellow slurry required much more time to dissolve at the higher CO pressure, and, as the slurry dissolved, the CO pressure dropped noticeably requiring more CO to be added. Upon completion of the addition, the syringe was carefully removed, and the solution was stirred for a total of 85 h under the CO pressure at 50 °C. The final reaction mixture was a clear, yellow solution which contained no aldehyde product, no reduced product, and no unreacted vinyl triflate by GC analysis.

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Carbonylation of Crotylpalladium Chloride Dimer. Under 45 psig of CO, a 5-mL THF solution of 0.239 g (0.821 mmol) of Bu_3SnH was added over 2 h to a 50 °C solution of 0.123 g (0.312 mmol) of crotylpalladium chloride dimer, 0.654 g (2.50 mmol) of triphenylphosphine, and 0.017 g (0.16 mmol) of ethylbenzene in 5 mL of THF. GC analysis of the final reaction mixture indicated a less than 2% yield of carbonylated product and a large peak corresponding to the reduced product, which was not quantified.

Carbonylation of 3-Deuterio-3-chlorocyclohexene. Under 45 psig of CO, a 10-mL solution of 0.966 g (3.20 mmol) of Bu_3SnH in THF was added over 2.5 h to a 50 °C solution of 0.351 g (2.99 mmol) of a 74:26 mixture of 3-deuterio- and 1-deuterio-3-chlorocyclohexene and 0.132 g (0.144 mmol, 3.81 mol %) of $Pd(PPh_3)_4$ in 10 mL of THF. Upon completion of the addition, GC analysis of the final reaction mixture indicated a 41% yield of β,γ-unsaturated aldehyde product and a 59% yield of cyclohexene. The volatile materials were collected by vacuum transfer. Deuterium NMR analysis of the solution indicated a 1:1 mixture of the 1-deuterio- and the 3-deuterio-3-formylcyclohexene as well as a 1:1 mixture of the 1-deuterio- and 3-deuterio-cyclohexene: ^2H NMR (THF, 30 MHz) δ 1.35 (s, 0.28 D, reduced: =C—CD), 2.31 (s, 0.21 D, aldehyde: =C—CD), 5.04 (s, 0.31 D, reduced: =CD), 5.30 (s, 0.20 D, aldehyde: =CD).

Carbonylation of 1-Deuterio-3-chlorocyclohexene. The reaction procedure described for the 3-deuterio enriched isomer was repeated by using 0.975 g (3.35 mmol) of Bu_3SnH, 0.356 g (3.03 mmol) of a 69:31 mixture of 1-deuterio- and 3-deuterio-3-chlorocyclohexene, and 0.133 g (0.115 mmol, 3.81 mol %) of $Pd(PPh_3)_4$. GC analysis of the final reaction mixture indicated a 49% yield of the β,γ-unsaturated aldehyde product and a 51% yield of the reduced product. The volatile materials were collected by vacuum transfer, and NMR analysis indicated a 1:1 mixture of the 1-deuterio- and the 3-deuterio-3-formylcyclohexene as well as a 1:1 mixture of the 1-deuterio- and 3-deuterio-cyclohexene: ^2H NMR (THF, 30 MHz) δ 1.35 (s, 0.25 D, reduced: =C—CD), 2.29 (s, 0.25 D, aldehyde: =C—CD), 5.03 (s, 0.26 D, reduced: =CD), 5.30 (s, 0.24 D, aldehyde:=CD).

Control Reaction: 3-Chloro-1-butene under Carbonylation Conditions with No Bu_3SnH. Under 45 psig of CO, a solution of 0.268 g (2.96 mmol) of 3-chloro-1-butene and 0.130 g (0.112 mmol, 3.80 mol %) of $Pd(PPh_3)_4$ in 10 mL of THF was stirred at 50 °C for 3 h. The volatiles were collected by vacuum transfer, and GC analysis indicated an isomer mixture of allylic chlorides: 51% yield of 3-chloro-1-butene and 49% yield of 1-chloro-2-butene. No product isolation was carried out.

3-Pentenal and 2-Pentenal, 2,4-Dinitrophenylhydrazones (30 and 31), from 1-Chloro-2-butene. Under 45 psig of CO, a 10-mL THF solution of 0.952 g (3.27 mmol) of Bu_3SnH was added over 3.5 h to a 50 °C solution of 0.277 g (3.06 mmol) of 1-chloro-2-butene and 0.137 g (0.119 mmol, 3.87 mol %) of $Pd(PPh_3)_4$ in 5 mL of THF. GC analysis of the final reaction mixture indicated a 12% yield of the carbonylated product, a 4:1 mixture of 3-pentenal and 2-pentenal. The reduced product was observed, but no yield was determined: GC/LRMS, *m/e* (relative intensity) 56 (M^+, 86%). The volatile materials were collected by vacuum transfer, and the solution was concentrated. The resulting residue was dissolved in 5 mL of absolute ethanol and added to a 2,4-dinitrophenylhydrazine solution (0.370 g [1.87 mmol] in 20 mL of absolute ethanol, 10 mL of water and 3 mL of concentrated sulfuric acid) to slowly form a fine red-orange precipitate. The mixture was stirred at room temperature for 2 h, cooled to 0 °C overnight, and filtered to afford 0.087 g (100% yield based on crude aldehyde) of 2,4-dinitrophenylhydrazone, a 1:4 mixture of 3- and 2-pentenal derivatives. The red-orange solid required no further purification: mp 131–136 °C; NMR ($CDCl_3$, 270 MHz) δ 1.12 (t, J = 7.5 Hz, 2.4 H, **31**: CH_3), 1.72–1.76 (m, 0.6 H, **30**: CH_3), 2.26–2.36 (m, 1.6 H, **31**: CH_2), 3.11–3.15 (m, 0.4 H, **30**: CH_2), 5.41–5.58 (m, 0.2 H, **30**: =CH), 5.59–5.80 (m, 0.2 H, **30**: =CH), 6.32–6.41 (m, 1.6 H, **31**: HC=CH), 7.49 (t, J = 5.5 Hz, 0.2 H, **30**: N=CH), 7.75–7.85 (m, 0.8 H, **31**: N=CH), 7.90–7.98 (m, 1 H, Ar H), 8.29 (dd, J = 9.4, 2.4 Hz, 1 H, Ar H), 9.10 (d, J = 2.5 Hz, 1 H, Ar H), 11.03 (br s, 0.2 H, **30**: NH), 11.09 (br s, 0.8 H, **31**: NH); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 12.6, 17.8, 26.0, 35.7, 116.6, 123.3, 124.1, 125.6, 129.5, 129.8, 138.1, 144.8, 145.2, 147.3, 150.3, 150.8; IR ($CDCl_3$) 3299, 1619, 1592, 1515, 1418, 1338 cm^{-1}. Anal. Calcd for $C_{11}H_{12}N_4O_4$: C, 50.00; H, 4.58; N, 21.20. Found: C, 49.89; H, 4.59; N, 21.19.

3-Pentenal and 2-Pentenal, 2,4-Dinitrophenylhydrazones (30 and 31) from 3-Chloro-1-butene. Under 45 psig of CO, a 10-mL THF solution of 0.981 g (3.37 mmol) of Bu_3SnH was added over 3.5 h to a 50 °C solution of 0.275 g (3.04 mmol) of 3-chloro-1-butene and 0.131 g (0.113 mmol, 3.73 mol %) of $Pd(PPh_3)_4$ in 5 mL of THF. GC analysis of the final reaction mixture indicated a 13% yield of the carbonylated product, a 4:1 mixture of 3-pentenal and 2-pentenal, and the reduced product was observed, but no yield was determined. The volatile materials were collected by vacuum transfer, and the solution was concentrated. The crude material was dissolved in 5 mL of absolute ethanol and added to a 2,4-dinitrophenylhydrazine solution (0.374 g [1.89 mmol] in 15 mL of absolute ethanol, 5 mL of water, and 3 mL of concentrated sulfuric acid), which slowly precipitated a yellow-orange solid. The mixture was stirred at room temperature for 1 h, cooled to 0 °C for 1 h, and filtered to afford 0.097 g (100% yield based on crude aldehyde) of 2,4-dinitrophenylhydrazone, a 3:1 mixture of 3- and 2-pentenal derivatives. The bright orange solid required no further purification: mp 89–95 °C; NMR ($CDCl_3$, 270 MHz) δ 1.12 (t, J = 7.4 Hz, 0.9 H, **31**: CH_3), 1.72–1.75 (m, 2.1 H, **30**: CH_3), 2.28–2.32 (m, 0.6 H, **31**: CH_2), 3.10–3.14 (m, 1.4 H, **30**: CH_2), 5.45–5.54 (m, 0.7 H, **30**: =CH), 5.56–5.82 (m, 0.7 H, **30**: =CH), 6.31–6.37 (m, 0.6 H, **31**: HC=CH), 7.47 (t, J = 5.5 Hz, 0.7 H, **30**: N=CH), 7.76–7.80 (m, 0.3 H, **31**: N=CH), 7.91–7.98 (m, 1 H, Ar H), 8.30 (dd, J = 9.5, 2.3 Hz, 1 H, Ar H), 9.12 (d, J = 2.5 Hz, 1 H, Ar H), 11.03 (br s, 0.7 H, **30**: NH), 11.09 (br s, 0.3 H, **31**: NH); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 12.6, 17.8, 26.0, 35.7, 116.5, 123.3, 124.1, 125.6, 129.5, 129.8, 138.1, 144.8, 145.2, 147.2, 150.3, 150.7; IR ($CDCl_3$) 3303, 1621, 1596, 1518, 1423, 1335 cm^{-1}; HRMS, calcd for $C_{11}H_{12}N_4O_4$: 264.0860. Found: 264.0854.

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